

coside therapy.⁶ This observation gives further support to a putative relationship between severe aminoglycoside toxicity and an elevation in the serum LDH_i levels. Although renal failure was attributed to aminoglycoside therapy, a renal biopsy was not done to provide conclusive proof for this diagnosis. In the absence of fever, rash, eosinophilia or eosinophiluria, a drug-induced interstitial nephritis from ce-fazolin would be unlikely but not impossible.⁷ Either antibiotic could have led to damaged renal tubular epithelium and have caused the release of renal LDH.

Elevations in serum LDH levels of renal origin have been attributed exclusively to embolic renal infarction,^{1,2} usually in patients with cardiomegaly and atrial fibrillation or myocardial infarction.⁷ Embolic occlusion of a renal artery can lead to complete unilateral renal infarction and elevation of the serum LDH level to 2,000 to 2,500 units per liter.⁷ In the present case, lack of a suitable clinical context and absence of a focal loss of renal parenchyma as shown by a renal isotope scan mitigated against embolic renal infarction and supported the diagnosis of antibiotic-induced acute renal insufficiency that caused release of renal LDH.

Young's Syndrome

An Association Between Male Sterility and Bronchiectasis

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IT HAS BEEN well established that there are associations between bronchiectasis or chronic bronchitis and male infertility.^{1,2} The best known examples are cystic fibrosis¹ and the immotile cilia syndrome.² Young's syndrome was described in 1970, consisting of chronic lung disease, obstructive azoospermia, normal spermatogenesis and characteristic epididymal findings.³ Unlike the immotile cilia syndrome, Young's syndrome is characterized by azoospermia and normal ultrastructure of cilia. It differs from cystic fibrosis by a normal sweat test and normal pancreatic function.⁴ We report the case of a patient with the clinical features of Young's syndrome.

Report of a Case

A 64-year-old man, white and a nonsmoker, started having recurrent lung infections at age 20. Since then he has had a chronic cough productive of one to two cups of yellowish sputum daily. A bronchogram done 30 years ago showed bilateral bronchiectasis. He has always had postnasal drip and a mucopurulent nasal discharge. He had normal sexual development, libido and potency. Despite being sexually active and married twice (8 and 11 years' durations), he has had no children. The patient used condoms, however,

In this patient, azotemia required dialysis and lasted several weeks, but the relationship, if any, of the elevation in renal LDH to the course and prognosis of the acute renal insufficiency remains unknown. Antibiotic-induced acute renal failure should be included in the differential diagnosis of an elevation in the serum LDH level, and isoenzyme fractionation should be done to help confirm that the LDH is of renal origin.

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ABBREVIATIONS USED IN TEXT

AAT = α_1 -antitrypsin
FEV₁ = forced expiratory volume in one second
FSH = follicle-stimulating hormone
FVC = forced vital capacity
Ig = immunoglobulin
TIC = trypsin inhibitory capacity

during his first marriage because children were not wanted; the second marriage has been to a postmenopausal woman six years his senior. There is no history of asthma, occupational exposure to toxins or scrotal trauma or infection, nor is there a family history of asthma, bronchitis, bronchiectasis, chronic lung disease or infertility.

On physical examination, he was well developed, well nourished and had mild clubbing of the fingers. Auscultation of the lungs showed early inspiratory crackles in both lower lung fields and mild diffuse wheezing. The external genitalia were normal with normal-sized testes of normal consistency and a palpable right epididymis and vas deferens. The left epididymis, however, was hypoplastic with cystic distention in the head.

Laboratory studies showed a slightly increased serum immunoglobulin (Ig) A level (646 mg per dl) and normal IgG and IgM values. A sputum culture grew *Hemophilus parainfluenzae*. A sweat test done by pilocarpine iontophoresis showed a normal sweat chloride value of 34 mEq per liter. α_1 -Antitrypsin (AAT) studies showed an MS phenotype and a serum trypsin inhibitory capacity (TIC) of 1.063 units per ml. The heterozygous S variant of AAT is not known to be associated with any disease state, and in this instance the associated serum TIC value is normal (>0.95 units per ml). The serum follicle-stimulating hormone (FSH) level was 11.0 mIU per ml (normal 1 to 15) and the testosterone level was 540 ng per dl (normal 400 to 1,000). Antisperm antibodies were absent from the serum. On semen analysis there was complete azoospermia.

Pulmonary function testing showed moderate obstructive

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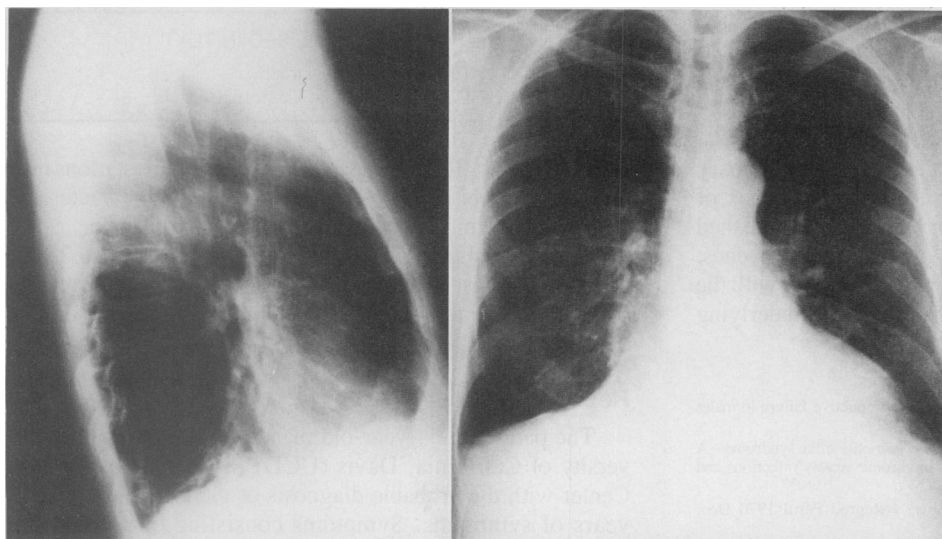


Figure 1.—Chest roentgenograms (left, lateral; right, posteroanterior) show peribronchial interstitial thickening in both lower lung fields.

lung disease with a forced expiratory volume in one second (FEV_1) of 1.34 liters (53% of predicted), a forced vital capacity (FVC) of 2.17 liters (58% of predicted) and an FEV_1/FVC ratio of 62%. The residual volume was 3.73 liters (157% of predicted) and total lung capacity was 6.42 liters (105% of predicted). Diffusing capacity was normal (98% of predicted).

The chest roentgenogram showed peribronchial interstitial thickening in both lower lung fields (Figure 1) while mucosal hypertrophy of the maxillary and frontal sinuses was shown in the sinus roentgenogram (Figure 2).

A test for the presence of cystic fibrosis lectin⁵ was also negative, ruling against a diagnosis of cystic fibrosis.

Discussion

In 1970 Young, in England, first reported 28 cases of patients with azoospermia associated with bronchitis or bronchiectasis.³ He called it Berry-Perkins-Young's syndrome. Sweat tests were not done, however, and it is possible that some of his patients might actually have had cystic fibrosis. Hendry and co-workers, also in England, studied 30 patients with obstructive azoospermia; 15 of the 30 patients also had sinusitis or bronchiectasis and the clinical features of Young's syndrome.⁶ The most recent study was by Handelsman and associates in Australia.⁴ They studied extensively 29 men with Young's syndrome and estimated that its prevalence among infertile men is comparable to that of Klinefelter's syndrome but higher than that of cystic fibrosis or the immotile cilia syndrome. These patients characteristically had chronic sinopulmonary infection starting in early childhood, with considerable symptomatic improvement after adolescence. Exercise capacity was either unlimited or only minimally impaired. Respiratory function testing indicated a mild increase in residual volume and a decrease in peak expiratory flow rate. All other lung volumes and gas exchange function were normal. They all had normal gonadal function but the epididymides were frequently enlarged or cystic (or both) in the region of the caput, which contained abundant spermatozoa. In the region of the corpus, the lumen was filled with amorphous inspissated secretions, but no sperm were present. The inspissated secretions were thought to be the cause of obstructive azoospermia.

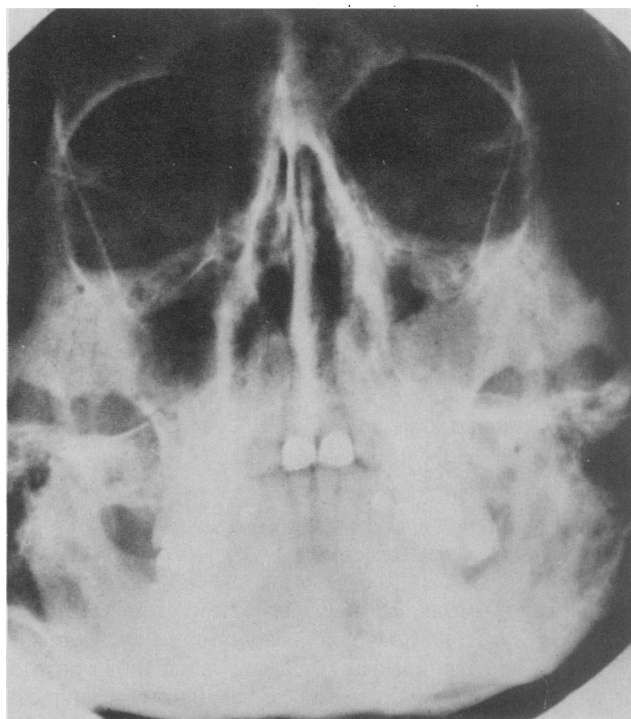


Figure 2.—A sinus roentgenogram shows mucosal hypertrophy of the maxillary and frontal sinuses.

There is no laboratory test for the diagnosis of Young's syndrome. The diagnosis is based on clinical grounds and the exclusion of cystic fibrosis and the immotile cilia syndrome.⁴

Our patient has chronic sinusitis, bronchiectasis, an abnormal epididymis and azoospermia. His normal serum FSH levels and testicular size suggest that spermatogenesis is normal.⁷ A negative sweat test usually rules out cystic fibrosis, as do the presence of palpable epididymides and vasa deferens and a negative cystic fibrosis lectin test. Azoospermia, on the other hand, is not compatible with the immotile cilia syndrome. Thus, he meets the criteria for the diagnosis of Young's syndrome.⁴ The unusual features in this case are the relatively late onset of lung problems at age 20 and his moderate obstructive lung disease.

Review of the English-language medical literature elicited very few reports of Young's syndrome. To our knowledge, no case of Young's syndrome has been reported in this country. The disease is probably overlooked and underreported because most patients have only mild respiratory disease that improves after adolescence, and nearly normal pulmonary function is usually found.⁴ The cause and pathogenesis of Young's syndrome are not known, nor has it been established to be a hereditary disease.⁸ Physicians dealing with chest disease and male fertility problems should be familiar with the syndrome. More studies are needed to uncover the underlying defect of this interesting syndrome.

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Glucagonoma—An Underdiagnosed Syndrome?

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ISLET CELL TUMORS are notoriously slow growing. In the early stages of growth, symptoms are minimal and atypical, while classic symptoms may occur only late in tumor growth or not at all. We report a case of a patient with atypical symptoms and signs for a 12-year period before the definitive diagnosis of glucagonoma was established.

Possible explanations for the atypicality of symptoms include (1) islet cell tumors may be composed of cells secreting more than one hormone, and these hormones may be synergistic or antagonistic; (2) secretion of one hormone, such as glucagon, may serve as a stimulus for hypersecretion of another, such as insulin; (3) pancreatic islet cell tumors may be only one component of a multiple endocrine neoplastic syn-

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ABBREVIATIONS USED IN TEXT

CT = computed tomography
UCD = University of California, Davis

drome (type I or II). The resulting clinical manifestations may thus be atypical or incomplete and lack the characteristic findings of the initially described "classic" syndrome.

Clinicians should be more alert to the forme fruste manifestations of these syndromes and less hesitant to order readily available radioimmunoassays even in the absence of some of the classic features.

Report of a Case

The patient, a 64-year-old man, was referred to the University of California, Davis (UCD) (Sacramento), Medical Center with the probable diagnosis of glucagonoma after 12 years of symptoms. Symptoms consisting of indigestion, post-meal nausea, sweating and weakness began at age 52. The patient was told he had "hypoglycemia," and he was placed on a high-protein, low-carbohydrate diet. At age 56, because of persisting symptoms, he was restudied and told he had mild diabetes mellitus. A regimen of an oral hypoglycemic agent (chlorpropamide [Diabinese]) was started. At age 57, a glucose tolerance test was repeated, and the patient was then told he did not have diabetes but that the original diagnosis of hypoglycemia was correct. The patient vividly recalled that during this test and about two hours after glucose administration, he had rather typical symptoms of hypoglycemia with sweating and weakness. Chlorpropamide administration was discontinued. At that time he began to have intermittent diarrhea. Physical examination was nonrevealing except for the detection of bilateral inguinal hernias, which were repaired. Dermatitis involving the groin, scrotal and perianal areas developed postoperatively. From this time (age 57) to age 64, the dermatitis was variable in nature, gradually becoming more generalized. Numerous dermatologists were consulted and biopsies done without a specific diagnosis being made. During this same period of time, the patient was having intermittent tongue and throat soreness, at times of such severity as to be associated with blister formation on his lips. Treatment was empiric and included administration of cimetidine, ranitidine and antacids for gastrointestinal complaints, and antihistaminics, adrenocorticotrophic hormone, skin ointments, nystatin, wet compresses and antibiotics for the dermatitis. The skin rash was diagnosed on different occasions as tinea cruris, neurodermatitis, fungal infection, staphylococcal infection and psoriasis. Results of diagnostic studies including upper gastrointestinal tract films, gallbladder x-ray films, colon x-ray films, sigmoidoscopy, gastroduodenoscopy, ultrasound of the abdomen and biopsy of skin lesions were nondiagnostic. Laboratory determinations, including complete blood count, fasting blood glucose levels and 20-chemistry and 8-chemistry panels, remained normal.

In late 1983 at age 64—12 years after the onset of symptoms—the patient was seen at the Sansum Medical Clinic in Santa Barbara where one of us (C.A.D.) recognized the symptoms of sore tongue, chronic indigestion and erythematous variable rash as being suggestive of a glucagon-secreting tumor. The serum glucagon level (BioScience Laboratories, Van Nuys, Calif) was greatly elevated at 2,400 pg per ml.